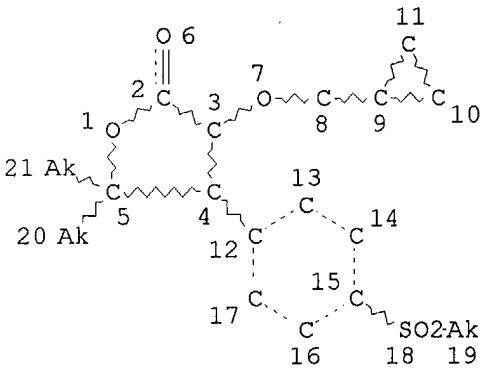
=> d que l4
L1 STR



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CONNECT IS E1 RC AT 19
CONNECT IS E1 RC AT 20
CONNECT IS E1 RC AT 21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE
L3 4 SEA FILE=REGISTRY SSS FUL L1
L4 14 SEA FILE=HCAPLUS ABB=ON PLU=ON L3

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L4 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:203410 HCAPLUS
DOCUMENT NUMBER: 138:226777
TITLE: Polymorphic B form of 3-(cyclopropylmethoxy)-4-[4(methylsulfonyl)phenyl]-5,5-dimethyl-5H-furan-2-one
INVENTOR(S): Calais, Beatrice; Chassagneux, Evelyne; Bonard, Jean-Michel
PATENT ASSIGNEE(S): Fr.
SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of Appl. No. PCT/EP00/10421.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003050337	A1	20030313	US 2002-117854	20020408
EP 1090915	A1	20010411	EP 1999-402482	19991008

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

WO 2001027097 A1 20010419 WO 2000-EP10421 20001009

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 1999-402482 A 19991008
WO 2000-EP10421 A2 20001009

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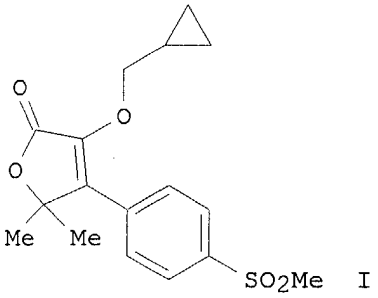


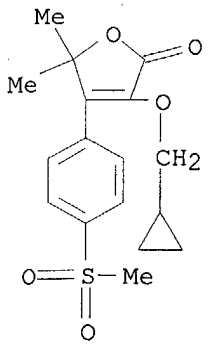
I

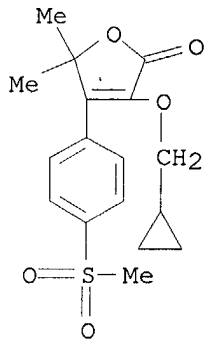
AB This invention is related to a polymorphic B Form of I. Polymorph A of I was converted to form B by stirring in methanol without seeding. Crystallog. data are given for form B.

IT **189954-96-9**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(polymorphic B form of 3-(cyclopropylmethoxy)-4-[4(methylsulfonyl)phenyl]-5,5-dimethyl-5H-furan-2-one)

RN 189954-96-9 HCAPLUS

CN 2(5H)-Furanone, 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)





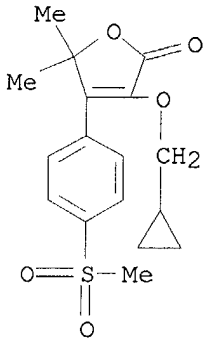
L4 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:850976 HCAPLUS
DOCUMENT NUMBER: 135:376778
TITLE: Combination therapy using COX-2 selective inhibitor and thromboxane inhibitor and compositions therefor
INVENTOR(S): Scolnick, Edward; Metters, Kathleen; Riendeau, Denis; Turner, Mervyn
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087343	A2	20011122	WO 2001-CA683	20010514
WO 2001087343	A3	20020926		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002016342	A1	20020207	US 2001-855061	20010514
EP 1283723	A2	20030219	EP 2001-933495	20010514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-204269P P 20000515
WO 2001-CA683 W 20010514

AB The present invention provides a method for the treatment or prophylaxis of COX-2 mediated conditions in patients who are at risk of developing thromboembolic events which comprises administering to said patient a therapeutically or prophylactically effective amt. of a COX-2 selective inhibitor and a cardiovascular protective amt. of a thromboxane inhibitor, as well as compns. therefor. A tablet contained thromboxane inhibitor 25.0, COX-2 selective inhibitor 25.0, microcryst. cellulose 37.25, modified food corn starch 37.25, and magnesium stearate 0.50 mg.

IT **189954-96-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy using COX-2 selective inhibitor and thromboxane inhibitor and compns. therefor)
RN 189954-96-9 HCAPLUS
CN 2(5H)-Furanone, 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:617863 HCAPLUS
DOCUMENT NUMBER: 135:200445
TITLE: Pharmaceutical or veterinary paste formulations containing silica and viscosity modifier
INVENTOR(S): Jun, Chen
PATENT ASSIGNEE(S): Merial Limited, UK
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

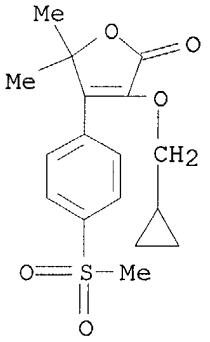
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060409	A1	20010823	WO 2001-EP1155	20010205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003007958	A1	20030109	US 2000-504741	20000216
EP 1263467	A1	20021211	EP 2001-905731	20010205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001008449	A	20030401	BR 2001-8449	20010205

JP 2003522805 T2 20030729 JP 2001-559505 20010205
PRIORITY APPLN. INFO.: US 2000-504741 A 20000216
WO 2001-EP1155 W 20010205

AB A pharmaceutical or veterinary paste formulation comprises a drug, fumed silica, a viscosity modifier, a hydrophilic carrier, optionally, an absorbent and a dye, stabilizer, surfactant, or preservative. This invention also provides for methods of using these formulations for treating various disease states as well. Thus, a paste was prepd. contg. 3-(cyclopropylmethoxy)-5,5-dimethyl-4-((4-methylsulfonyl)phenyl)-5H-furan-2-one (COX-2 inhibitor) 0.82, TiO2 0.2, MgCO3 2, fumed silica 4.25, and PEG-300 0.4% and triacetin qs.

IT **189954-96-9**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical or veterinary paste formulations contg. silica and viscosity modifier)

RN 189954-96-9 HCAPLUS
CN 2(5H)-Furanone, 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



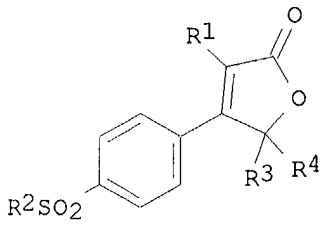
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:283940 HCAPLUS
DOCUMENT NUMBER: 134:295732
TITLE: Preparation of (4-alkylsulfonyl)phenyl-2(5H)-furanones as COX-2 inhibitors
INVENTOR(S): Canali, Laetitia; Cruciani, Paul; Oddon, Gilles
PATENT ASSIGNEE(S): Merial, Fr.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027098	A2	20010419	WO 2000-FR2770	20001005
WO 2001027098	A3	20010830		

W: AU, CA, JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
FR 2799462 A1 20010413 FR 1999-12583 19991008
EP 1218366 A2 20020703 EP 2000-967956 20001005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY
US 2003028036 A1 20030206 US 2002-117832 20020408
US 6541646 B2 20030401
PRIORITY APPLN. INFO.: FR 1999-12583 A 19991008
WO 2000-FR2770 W 20001005
OTHER SOURCE(S): MARPAT 134:295732
GI



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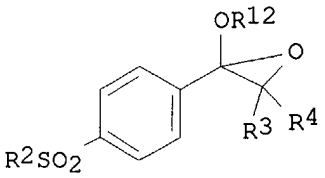


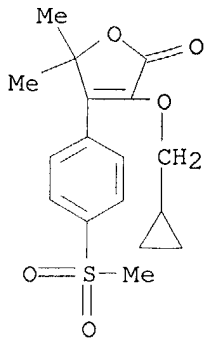
II

AB The title compds. I (R1 = OR5, R5, mono-, di-, or tri-substituted Ph, etc.; R2 = (C1-C6)alkyl; R3, R4 = H, CHR6R7), COX-2 inhibitors, were prepd. The method is characterized in that it comprises the following steps: (a) reacting a compd. of general formula II with an acid of general formula R1CH2COOH in a water-free medium; (b) reacting the resulting compd. with a strong base in an aprotic solvent in order to obtain an intermediate cyclic compd. which forms a compd. of general formula I after dehydration; and (c) isolating said resulting compd. of general formula I. E.g., a multistep synthesis of 3-(cyclopropylmethoxy)-5,5-dimethyl-4-(4'-methylsulfonylphenyl)-5H-furan-2-one from 4-methylthioisobutyrophenone is reported.

IT **189954-96-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (alkylsulfonyl)phenylfuranones as COX-2 inhibitors)

RN 189954-96-9 HCAPLUS

CN 2(5H)-Furanone, 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:261096 HCAPLUS
DOCUMENT NUMBER: 134:271286
TITLE: Polymorphic B form of 3-(cyclopropylmethoxy)-4-[-4-(methylsulfonyl)phenyl]-5,5-dimethyl-5H-furan-2-one
INVENTOR(S): Calais, Beatrice; Chassagneux, Evelyne; Bonard, Jean-Michel
PATENT ASSIGNEE(S): Merial, Fr.
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

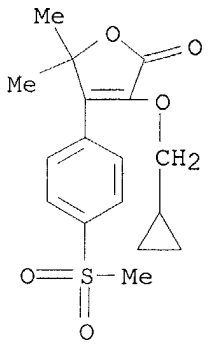
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1090915	A1	20010411	EP 1999-402482	19991008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2001027097	A1	20010419	WO 2000-EP10421	20001009
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2003511443	T2	20030325	JP 2001-530316	20001009
US 2003050337	A1	20030313	US 2002-117854	20020408

PRIORITY APPLN. INFO.: EP 1999-402482 A 19991008
WO 2000-EP10421 W 20001009

AB A polymorphic B form of 3-(cyclopropylmethoxy)-4-[4-(methylsulfonyl)phenyl]-5,5-dimethyl-5H-furan-2-one (I) is characterized by the powder x-ray diffraction pattern. Thus, the polymorph A of I was recrystd. to give a polymorph B from a 30% soln. in THF/methylcyclohexane.

IT **189954-96-9**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymorphic form of cyclopropylmethoxy(methylsulfonyl)phenyldimethylfu

ranone)
RN 189954-96-9 HCAPLUS
CN 2(5H)-Furanone, 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

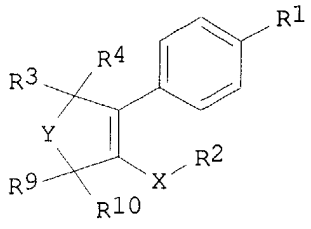
L4 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:83114 HCAPLUS
DOCUMENT NUMBER: 132:122509
TITLE: Preparation of (methylsulfonyl)phenyl-2-(5H)-furanones as COX-2 inhibitors
INVENTOR(S): Belley, Michel; Gauthier, Jacques Yves; Grimm, Erich; Leblanc, Yves; Li, Chun-sing; Therien, Michel; Black, Cameron; Prasit, Petpiboon; Lau, Cheuk-kun; Roy, Patrick
PATENT ASSIGNEE(S): Merck Frosst Canada, Inc., Can.
SOURCE: U.S., 88 pp., Cont.-in-part of U.S. Ser. No. 728,512, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6020343	A	20000201	US 1998-97543	19980615
NZ 332820	A	20000526	NZ 1996-332820	19961009
JP 2001199954	A2	20010724	JP 2000-366579	19961009
ZA 9608609	A	19970414	ZA 1996-8609	19961011
US 6169188	B1	20010102	US 1999-422151	19991021

PRIORITY APPLN. INFO.:
US 1995-5371P P 19951013
US 1996-11637P P 19960214
US 1996-728512 B2 19961009
GB 1996-2939 A 19960213
GB 1996-5645 A 19960318
JP 1997-515371 A3 19961009
NZ 1996-319090 A1 19961009
US 1998-97543 A3 19980615

OTHER SOURCE(S): MARPAT 132:122509

GI



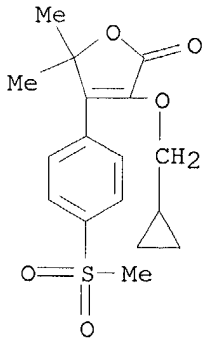
I

AB The title compds. [I; X = CH2, CHOH, CO, etc.; Y = O, S, CO, etc.; R1 = SO2Me, SO2NHCOCF3, SONHNH2, etc.; R2 = alkyl, (un)substituted Ph, naphthyl, etc.; R3 = H, alkyl, CN, etc.; R4 = H, alkyl, alkoxy, etc.; R9, R10 = H, alkyl; R9 and R10 together with the carbon atom to which they are attached form a carbonyl or thiocarbonyl group], useful in the treatment of cyclooxygenase-2 mediated diseases such as inflammation, arthritis, osteoporosis, rheumatoid arthritis, and pain, were prepd. E.g., a 4-step synthesis of I [X = O; Y = O; R1 = SO2Me; R2 = 3,4-F2C6H3; R3 = R4 = Me; R9 and R10 together with the carbon atom to which they are attached form a carbonyl group] which showed ED50 of 0.14 mg/kg in rat paw edema assay, was given.

IT **189954-96-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (methylsulfonyl)phenyl-2-(5H)-furanones as COX-2 inhibitors)

RN 189954-96-9 HCAPLUS

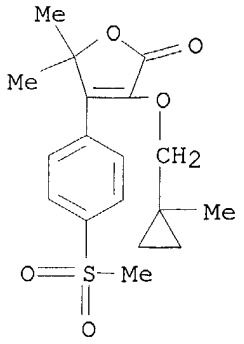
CN 2(5H)-Furanone, 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



IT **189955-18-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of (methylsulfonyl)phenyl-2-(5H)-furanones as COX-2 inhibitors)

RN 189955-18-8 HCAPLUS

CN 2(5H)-Furanone, 5,5-dimethyl-3-[(1-methylcyclopropyl)methoxy]-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:753114 HCAPLUS
DOCUMENT NUMBER: 132:6353
TITLE: Use of a COX-2 inhibitor and a NK-1 receptor antagonist for treating inflammation
INVENTOR(S): Boyce, Susan; Hill, Raymond George; Rupniak, Nadia Melanie
PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9959635	A1	19991125	WO 1999-GB1632	19990519
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2327585	AA	19991125	CA 1999-2327585	19990519
AU 9939486	A1	19991206	AU 1999-39486	19990519
AU 758983	B2	20030403		
EP 1079863	A1	20010307	EP 1999-922393	19990519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002515461	T2	20020528	JP 2000-549299	19990519

PRIORITY APPLN. INFO.: GB 1998-10920 A 19980521
WO 1999-GB1632 W 19990519

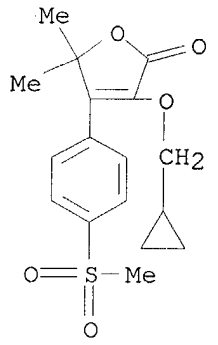
OTHER SOURCE(S): MARPAT 132:6353

AB The present invention provides the use of a COX-2 inhibitor and a NK-1 receptor antagonist for the manuf. of a medicament for the treatment or prevention of inflammatory disorders, methods of treatment using the COX-2 inhibitor and NK-1 receptor antagonist and pharmaceutical compns. and products contg. them. One example NK-1 antagonist is 2R-[1R-[3,5-bis(trifluoromethyl)phenyl]ethoxy]3S-(4-fluorophenyl)-4-[3-(5-oxo-1H,4H-1,2,4-triazolo)methyl]morpholine. Tablet formulations were given.

IT **189954-96-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(COX-2 inhibitor and a NK-1 receptor antagonist for treating inflammation)

RN 189954-96-9 HCAPLUS

CN 2(5H)-Furanone, 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:718982 HCAPLUS

DOCUMENT NUMBER: 131:322532

TITLE: Preparation of 4-aryl-(5H)-furan-2-ones as cyclooxygenase-2 inhibitors.

INVENTOR(S): Belley, Michel; Gauthier, Jacques Yves; Grimm, Erich; Leblanc, Yves; Li, Chun-Sing; Therien, Michel; Black, Cameron; Prasit, Petpiboon; Lau, Cheuk-Kun; Roy, Patrick

PATENT ASSIGNEE(S): Merck Frosst Canada, Inc., Can.

SOURCE: U.S., 74 pp., Cont.-in-part of U.S. Ser. No. 728,512, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

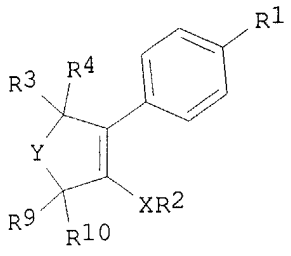
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5981576	A	19991109	US 1998-97537	19980615
NZ 332820	A	20000526	NZ 1996-332820	19961009
JP 2001199954	A2	20010724	JP 2000-366579	19961009

ZA 9608609	A	19970414	ZA 1996-8609		19961011
PRIORITY APPLN. INFO.:			US 1995-5371P	P	19951013
			US 1996-11637P	P	19960214
			US 1996-728512	B2	19961009
			GB 1996-2939	A	19960213
			GB 1996-5645	A	19960318
			JP 1997-515371	A3	19961009
			NZ 1996-319090	A1	19961009

OTHER SOURCE(S): MARPAT 131:322532
GI



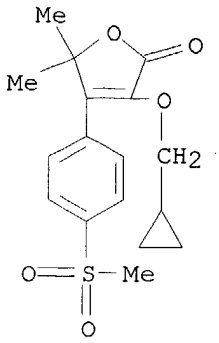
I

AB Title compds. [I; X = CH2, CH(OH), CO, O, S, NR15; Y = CO, O, S, CR11R12; R1 = SO2Me, SO2NR16R17, SO2NHCOCF3, etc.; R2 = alkyl, (substituted) Ph, naphthyl, heteroaryl, benzoheterocyclyl, heterocyclylalkyl, benzocarbocyclyl, etc.; R3 = H, alkyl, CH2OR7, cyano, CH2CN, (substituted) Ph, etc.; R4 = H, alkyl, alkoxy, alkylthio, OH, SH, OCOR7, etc.; R3R4 = atoms to form a 3-7 membered ring; R7 = H, alkyl, (substituted) Ph, PhCH2; R9, R10 = H, alkyl; R9R10 = O, S; R16, R17 = H, alkyl, alkanoic acid, alkyl amine, etc.; with provisos], were prepd. Thus, cyclopropanemethanol in THF was added to NaH in THF at 12.degree. over 75 min. followed by 18 h stirring at room temp.; ClCH2CO2Na was added followed by 8.5 h reflux to give an oil. This was refluxed with 2-bromo-2-methyl-1-[(4-methylsulfonyl)phenyl]propan-1-one (prepn. given) and ethyldiisopropylamine in EtOH to give cyclopropylmethoxyacetic acid 2-methyl-1-[(4-methylsulfonyl)phenyl]propan-1-one ester. The latter was refluxed with iso-Pr trifluoroacetate and DBU in MeCN to give 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[(4-methylsulfonyl)phenyl]-5H-furan-2-one. I inhibited rat paw edema with ED50 = 0.32-10 mg/kg orally.

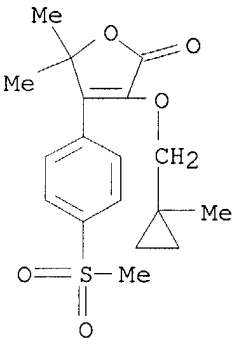
IT **189954-96-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-aryl-(5H)-furan-2-ones as cyclooxygenase-2 inhibitors)

RN 189954-96-9 HCAPLUS

CN 2(5H)-Furanone, 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



IT **189955-18-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of 4-aryl-(5H)-furan-2-ones as cyclooxygenase-2 inhibitors)
RN 189955-18-8 HCAPLUS
CN 2(5H)-Furanone, 5,5-dimethyl-3-[(1-methylcyclopropyl)methoxy]-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:594916 HCAPLUS
DOCUMENT NUMBER: 131:209130
TITLE: Combination therapy and composition using an antiplatelet agent and a COX-2 inhibitor for acute coronary ischemic syndrome and related conditions
INVENTOR(S): Nichtberger, Steven A.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9945913	A1	19990916	WO 1999-US5063	19990309
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2322824	AA	19990916	CA 1999-2322824	19990309
EP 1061908	A1	20001227	EP 1999-911208	19990309
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002506024	T2	20020226	JP 2000-535328	19990309
US 6136804	A	20001024	US 1999-267287	19990312
US 6511968	B1	20030128	US 2000-694212	20001023

PRIORITY APPLN. INFO.:

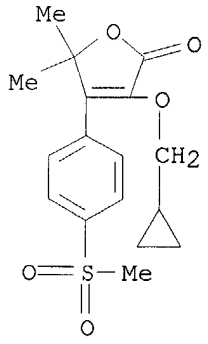
US 1998-77900P	P	19980313
GB 1998-15857	A	19980721
WO 1999-US5063	W	19990309
US 1999-267287	A3	19990312

AB A method for treating, preventing, or reducing the risk of developing a condition selected from acute coronary ischemic syndrome, thrombosis, thromboembolism, thrombotic occlusion and reocclusion, restenosis, transient ischemic attack, and first or subsequent thrombotic stroke, in a patient comprises administering to the patient a therapeutically effective amt. of an antiplatelet agent in combination with a therapeutically effective amt. of a COX-2 inhibitor. The invention also provides a pharmaceutical compn. comprising a therapeutically effective amt. of a COX-2 inhibitor, or a pharmaceutically acceptable salt thereof, and an antiplatelet agent, or a pharmaceutically acceptable salt thereof.

IT **189954-96-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiplatelet agent-cyclooxygenase-2 inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)

RN 189954-96-9 HCAPLUS

CN 2(5H)-Furanone, 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:536686 HCAPLUS
DOCUMENT NUMBER: 131:286347

TITLE: SAR in the alkoxy lactone series: the discovery of DFP, a potent and orally active COX-2 inhibitor

AUTHOR(S): Leblanc, Y.; Roy, P.; Boyce, S.; Brideau, C.; Chan, C. C.; Charleson, S.; Gordon, R.; Grimm, E.; Guay, J.; Leger, S.; Li, C. S.; Riendeau, D.; Visco, D.; Wang, Z.; Webb, J.; Xu, L. J.; Prasit, P.

CORPORATE SOURCE: Merck Frosst Centre for Therapeutic Research, Pointe Claire-Dorval, QC, H9R 4P8, Can.

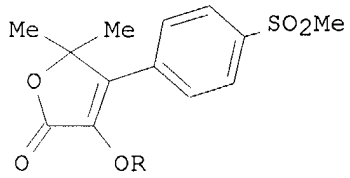
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(15), 2207-2212
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



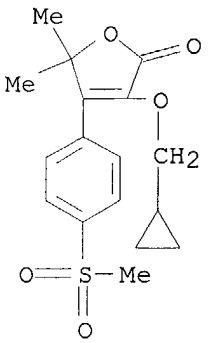
I

AB A structure-activity relationship has been established in the alkoxy lactone series I (R = cyclohexyl, cyclopentyl, cyclobutyl, cyclopropyl, s-Bu, 3-pentyl, Me, Et, i-Pr, cyclopropylmethyl, 1-cyclopropylethyl). This has led to the discovery of 5,5-dimethyl-3-(2-propyloxy)-4-[(methylsulfonyl)phenyl]-2(5H)-furanone (DFP; I, R = i-Pr), a highly selective potent COX-2 cyclooxygenase inhibitor exhibiting in vivo efficacy in all models studied.

IT **189954-96-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and SAR of dimethyl(alkyloxy)[(methylsulfonyl)phenyl]furanones as COX-2 inhibitors)

RN 189954-96-9 HCAPLUS

CN 2(5H)-Furanone, 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:282039 HCAPLUS
DOCUMENT NUMBER: 130:306593
TITLE: Combination therapy using a HMG-CoA reductase inhibitor and a cyclooxygenase-2 (COX-2) inhibitor for reducing the risks associated with cardio- and cerebrovascular disease
INVENTOR(S): Winokur, Melvin
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

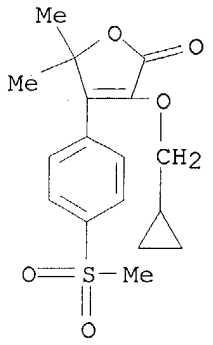
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920110	A1	19990429	WO 1998-US21901	19981016
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306646	AA	19990429	CA 1998-2306646	19981016
AU 9913612	A1	19990510	AU 1999-13612	19981016
AU 753657	B2	20021024		
EP 1024696	A1	20000809	EP 1998-957328	19981016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2001520174	T2	20011030	JP 2000-516533	19981016
US 6245797	B1	20010612	US 1998-179349	19981020

PRIORITY APPLN. INFO.: US 1997-62691P P 19971022
GB 1998-6688 A 19980327
WO 1998-US21901 W 19981016

AB The invention provides a drug combination comprised of a HMG-CoA reductase inhibitor in combination with a COX-2 inhibitor, which is useful for treating, preventing, and/or reducing the risk of developing atherosclerosis and atherosclerotic disease events. Prepn. of selected COX-2 inhibitors, e.g. 5-chloro-3-(4-methylsulfonyl)phenyl-2-(2-methyl-5-pyridinyl)pyridine, is described. Pharmaceutical formulations are included.

IT **189954-96-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HMG-CoA reductase inhibitor combination with COX-2 inhibitor for reducing risks assocd. with cardio- and cerebrovascular disease, COX-2 inhibitor prepn., and pharmaceutical formulations)

RN 189954-96-9 HCAPLUS
CN 2(5H)-Furanone, 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



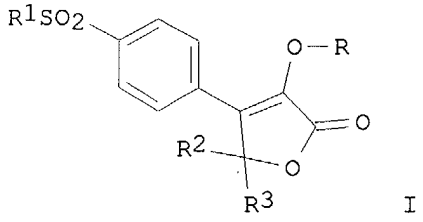
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:635753 HCAPLUS
DOCUMENT NUMBER: 129:275831
TITLE: Preparation of 4-[4-(methylsulfonyl)phenyl]-2-(5H)-furanones with oxygen link as COX-2 inhibitors
INVENTOR(S): Leblanc, Yves; Roy, Patrick; Leger, Serge; Grimm, Erich; Wang, Zhaoyin
PATENT ASSIGNEE(S): Merck Frosst Canada Inc., Can.
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9841516	A1	19980924	WO 1998-CA225	19980312
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9867142	A1	19981012	AU 1998-67142	19980312
AU 741981	B2	20011213		
EP 970067	A1	20000112	EP 1998-912164	19980312
EP 970067	B1	20030702		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001514668	T2	20010911	JP 1998-539978	19980312
AT 244232	E	20030715	AT 1998-912164	19980312
US 6071954	A	20000606	US 1998-42168	19980313

PRIORITY APPLN. INFO.: US 1997-40794P P 19970314
GB 1997-7488 A 19970414
WO 1998-CA225 W 19980312

OTHER SOURCE(S): MARPAT 129:275831
GI



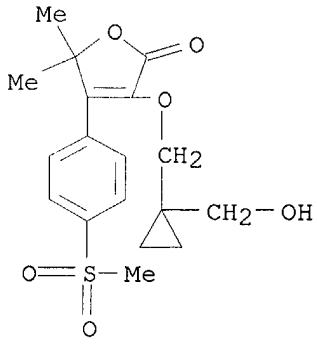
I

AB The title compds. [I; R = (un)substituted C1-12 alkyl, C2-10 alkenyl, C2-10 alkynyl, etc.; R1 = Me, NH2, NHC(O)CF3, NHMe; R2, R3 = H, C1-10 alkyl; R2R3 together with the carbon to which they are attached form a satd. C3-7 monocyclic ring], useful in the treatment of an inflammatory disease susceptible to treatment with an non-steroidal antiinflammatory agent, and for treating cyclooxygenase mediated diseases, were prepd. Thus, 6-step synthesis of I [R = CH(Me)CH:CH2; R1 = Me; R2 = R3 = Me] which showed IC50 of 0.05 .mu.M against COX-2 in CHO transfected cell lines, was described.

IT **213833-58-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 4-[4-(methylsulfonyl)phenyl]-2-(5H)-furanones with oxygen link as COX-2 inhibitors)

RN 213833-58-0 HCAPLUS

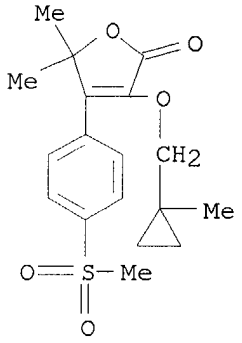
CN 2(5H)-Furanone, 3-[[1-(hydroxymethyl)cyclopropyl]methoxy]-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



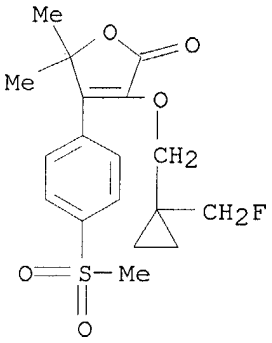
IT **189955-18-8P 213833-60-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-[4-(methylsulfonyl)phenyl]-2-(5H)-furanones with oxygen link as COX-2 inhibitors)

RN 189955-18-8 HCAPLUS

CN 2(5H)-Furanone, 5,5-dimethyl-3-[(1-methylcyclopropyl)methoxy]-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



RN 213833-60-4 HCAPLUS
CN 2(5H)-Furanone, 3-[[1-(fluoromethyl)cyclopropyl]methoxy]-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:425272 HCAPLUS
DOCUMENT NUMBER: 127:34112
TITLE: Preparation of 3,4-diaryl-2-hydroxy-2,5-dihydrofurans as prodrugs to cyclooxygenase-2 (cox-2) inhibitors and as non-steroidal anti-inflammatory agents
INVENTOR(S): Black, Cameron; Leger, Serge; Prasit, Petpiboon; Wang, Zhaoyin; Hamel, Pierre; Han, Yongxin; Hughes, Gregory
PATENT ASSIGNEE(S): Merck Frosst Canada Inc., Can.; Black, Cameron; Leger, Serge; Prasit, Petpiboon; Wang, Zhaoyin; Hamel, Pierre; Han, Yongxin; Hughes, Gregory
SOURCE: PCT Int. Appl., 213 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9716435	A1	19970509	WO 1996-CA717	19961029
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5698584	A	19971216	US 1996-738143	19961025
AU 9672736	A1	19970522	AU 1996-72736	19961029
AU 711902	B2	19991021		
JP 11500748	T2	19990119	JP 1996-516943	19961029
EP 904269	A1	19990331	EP 1996-934267	19961029
EP 904269	B1	20020123		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, LI, LU, NL, SE, PT, IE, FI				
AT 212343	E	20020215	AT 1996-934267	19961029
ES 2171723	T3	20020916	ES 1996-934267	19961029
JP 3337477	B2	20021021	JP 1997-516943	19961029
US 6057319	A	20000502	US 1998-68139	19981002

PRIORITY APPLN. INFO.: US 1995-8074P P 19951030
GB 1996-2877 A 19960213
WO 1996-CA717 W 19961029

OTHER SOURCE(S): MARPAT 127:34112

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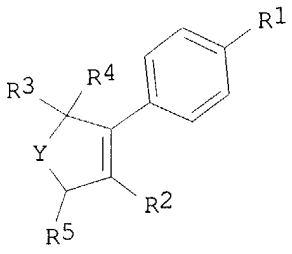


I

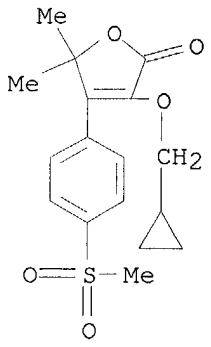
AB The invention encompasses the novel compd. of formula [I; Y = (un)substituted CH2, O, S, CO; R2 = SO2Me, (un)substituted SO2NH2, SO2NHCOCF3, SONHNH2, SONHNHCOCF3, P(O)MeNH2, P(O)Me2, C(S)NH2; R2 = NR10R11, SR11, OR11, R11, C1-10 alkenyl, C1-10 alkynyl, (un)substituted C3-10 cycloalkenyl; wherein R11 = C1-10 alkyl, C3-10 cycloalkyl, (un)substituted Ph, naphthyl, or heteroaryl, etc.; R3 = H, C1-10 alkyl, cyano, CH2CN, C1-6 fluoroalkyl, F, CH2OR8, CON(R8)2; R4 = H, C1-10 alkyl, C1-10 alkoxy, C1-10 alkylthio, OH, O2CR8, SH, SCOR8, OCO2R8, O CON(R8)2, SCON(R8)2, C3-10 cycloalkoxy or cycloalkylthio; or CR3R4 = 3- to 7-membered monocyclic ring optionally contg. 1 or 2 heteroatoms selected from O, S, or N; wherein R8 = H, C1-10 alkyl, C1-10 alkyl-CO2H, C1-10 aminoalkyl, (un)substituted Ph or CH2Ph, C3-10 cycloalkyl, C1-10 alkanoyl, (un)substituted benzoyl; R5 = OR17, SR18, NR17R18, S(O)R18, SO2 R18, SO2N(R17)2, OP(O)(OR16)2; wherein R16 = H, C1-6 alkyl, (un)substituted CH2Ph; R17 = H, R18; R18 = C1-10 alkyl, C1-10 alkyl-CO2H, C1-10 aminoalkyl, (un)substituted Ph or CH2Ph, C3-10 cycloalkyl,

(CH2CH2O)nH (n = 1-6), C1-10 alkanoyl, (un)substituted benzoyl]. They are in vivo converted into the active lactone form, i.e. arylhydroxydihydrofuranone derivs. I (R5 = oxo; Y, R1 - R4 = same as above) with high inhibitory activity against cyclooxygenase-2 and/or a specificity for cyclooxygenase-2 over cyclooxygenase-1 and useful in the treatment of cyclooxygenase-2 mediated diseases, in particular inflammatory diseases. Thus, 3,4-difluorophenoxyacetic acid was cyclocondensed with 2-hydroxy-4'-(methylsulfonyl)isobutyrophenone (prepn. given) using 1-cyclohexyl-3-(2-morpholinoethyl)carbodiimide metho-p-toluenesulfonate and 4-dimethylaminopyridine in CH2Cl2 at room temp. for 18 h to give 3-(3,4-difluorophenoxy)-5,5-dimethyl-4-(4-methylsulfonylphenyl)-5H-furan-2-one, which was reduced by (Me2CHCH2)2AlH in THF at room temp. for 30 min to give I (Y = O, R2 = 3,4-difluorophenoxy, R3 = R4 = Me, R5 = OH). The latter compd. showed ED50 of 0.09 mg/kg p.o. for inhibiting the carrageenan-induced paw edema in rats.

IT **189954-96-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diarylhydroxydihydrofurans as prodrugs for antiinflammatory diarylhydroxydihydrofuranones and selective cyclooxygenase-2 inhibitors)

RN 189954-96-9 HCAPLUS

CN 2(5H)-Furanone, 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1997:384238 HCAPLUS

DOCUMENT NUMBER: 127:5002

TITLE: (Methylsulfonyl)phenyl-2-(5H)-furanones as cox-2 inhibitors

INVENTOR(S): Belley, Michel; Gauthier, Jacques Y.; Grimm, Erich; Leblanc, Yves; Li, Chung-Sing; Therien, Michel; Black, Cameron; Lau, Cheuk-Kun; Prasit, Petpiboon; et al.

PATENT ASSIGNEE(S): Can.

SOURCE: PCT Int. Appl., 264 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9714691	A1	19970424	WO 1996-CA682	19961009
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OTHER SOURCE(S): MARPAT 127:5002
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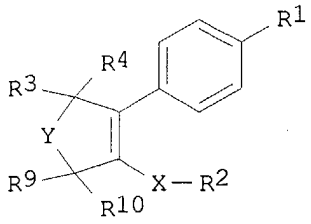


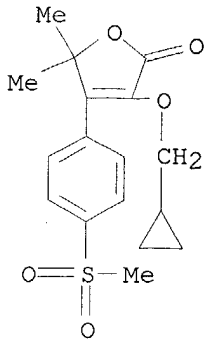
I

AB The title compds. [I; X = CH2, CHOH, CO, O, S, NR15 with the proviso that when R3 and R4 are other than both H, both C1-10 alkyl, or joined together with the carbon to which they are attached to form a satd. monocyclic carbon ring of 3, 4, 5, 6 or 7 atoms, then X is selected from CO, O, S, or NR15; Y = CR11R12, CO, O, S; R11, R12 = H, mono- or disubstituted Ph or mono- or disubstituted benzyl or mono- or disubstituted heteroaryl or mono- or disubstituted heteroarylmethyl wherein the substituents are H, halo, C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, etc.; R1 = SO2-Me, SO2-NR16R17, SO2-NH-CO-CF3, SONH-NH2, etc.; R2 = H, halo, C1-10 alkyl, mono- or disubstituted Ph or naphthyl wherein the substituents are selected from the group consisting of H, halo, C1-10 alkoxy, C1-10 alkylthio, etc.; R3 = H, C1-10 alkyl, CH2-OR7, CN, CH2CN, C1-6 fluoroalkyl, F, etc.; R4 = H, C1-10 alkyl, C1-10 alkoxy, C1-10 alkylthio, OH, etc.; R9, R10 = H, C1-7 alkyl, or R9R10 together with the carbon atom they are attached form a carbonyl or thiocarbonyl group; R15 = H, C1-10 alkyl, mono-, di-, or trisubstituted Ph or naphthyl, etc.; R16, R17 = H, C1-10 alkyl, alkanoic acid, alkyl amine, etc.] are prepd. Thus, 2-methyl-1-[4-(methylthio)phenyl]-1-propanone (prepd. from isobutyryl chloride and thioanisole) was treated with Aliquat 336 to give the 2-hydroxy deriv., which was oxidized to the sulfonyl compd. with Oxone, which was reacted with 3,4-difluorophenoxyacetic acid to give I [R1 = SO2-Me, R2 = 3,4-difluorophenyl, R3 = R4 = Me, R9R10 = O, X = Y = O]. In a red paw edema assay (using rats) for its antiinflammatory potency, this had ED50 of 0.14 mg/Kg. The invention also describes pharmaceutical compns. comprising I for treatment of cyclooxygenase-2 mediated diseases.

IT **189954-96-9P 189955-18-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
((methylsulfonyl)phenyl(5H)-furanones as cox-2 inhibitors)

RN 189954-96-9 HCAPLUS

CN 2(5H)-Furanone, 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



RN 189955-18-8 HCAPLUS
CN 2(5H)-Furanone, 5,5-dimethyl-3-[(1-methylcyclopropyl)methoxy]-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)